Allergic and Atopic Dermatitis
What’s New, What Works

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Chronic Pruritus
Problem and Opportunity

- In chronic or relapsing cases, your next dose of “pred” will be less effective than your predecessor
- “Just pred” approach is MAJOR source of client loss
- No dermatologist can do these cases in < one hour. Don’t try
- Be systematic
  - History
  - Tape and scrape every case
  - Protocol based. Don’t vary for individuals
  - Have and explain plan A and B
What is Atopic Dermatitis

- Genetically predisposed T cell disease
- Inappropriate response to environmental allergens
- Primary or secondary barrier defect.
- Most common veterinary disease in Australia.

Dietary Allergy
- Infection +/- yeast and staph allergy
- Drying of skin
- Barrier defect = increased allergen access

ITCH
Diagnosis of Atopic Dermatitis

1. **Typical Signs**

2. **Exclusion of other diseases**
   - Fleas
   - Food
   - Sarcoptes
   - Infection
   - CATS – Ringworm and psychogenic

Presentation and signs are often clinically indistinguishable from “DIETARY ALLERGY”. Alternative or concurrent diagnosis.

Criteria for the diagnosis of atopic dermatitis Favrot 2009

1. Onset of signs under 3 years of age
2. Mostly indoors
3. Glucocorticoid-responsive pruritus
4. Pruritus without lesions at onset
5. Affected front feet
6. Affected ear pinnae
7. Non-affected ear margins
8. Non-affected dorso-lumbar area

Five satisfied criteria sensitivity of 85% specificity of 79%
Six criteria sensitivity 89% Specificity 58%
Exclusion of ectoparasites increases specificity
Flea bite allergy  Sarcoptes

Cutaneous adverse food reactions
“Food allergy”
Cats - Atopic Dermatitis

- Miliary Dermatitis
- Allergic Alopecia – Pruritus
- Eosinophilic plaque
- Eosinophilic Granuloma Complex
- "Head and Neck Pruritus"
- Uricaria Pigmentosa
- Persian facial dermatitis?

All have similar etiologies
Similar diagnostic strategy
Similar therapeutics
Hnilica 2009

Caution

- Atopic dermatitis (or dietary allergy) may present as otitis without other symptoms and occasionally unilateral!
- Hydrolysed diet trials will miss up to 25% of food allergies
- In cats, dermatophytosis may present as a pruritic dermatitis. Only 50% of M. canis strains are Wood's Light positive.

Don’t get caught Toothbrush test all suspect cats
Five + 1/2 Pillars Approach to Atopic Dermatitis

1. Symptomatic immunosuppressive drugs
   • Corticosteroids
   • Cyclosporine

2. Allergen specific immunotherapy (ASIT) “Desensitization”

3. Infection control

4. Skin hydration and barrier repair. Moisturizing

5. Control other allergies (diet, fleas)

5&1/2.
   • Essential fatty acid therapy
   • Allergen avoidance
   • Antihistamines ??

Corticosteroids

Plus metabolic effects through receptors on most tissues
Corticosteroids

- Highly effective
- Failure to respond to corticosteroids usually indicates that either:
  1. The diagnosis of atopic dermatitis is not correct
  2. The atopic dermatitis is complicated by secondary infection

- There is no “safe” dose of prednisolone but dogs maintained on 0.25-0.5 mg/kg twice weekly have a reduced risk of side effects
- The cheap cost of prednisolone may soon be overtaken by the cost of its side effects
Hemodynamic effects of methylprednisolone acetate in cats.

- 5mg/mg methylprednisolone acetate (MPA)
- Substantial increase in serum glucose concentration at 3 to 6 days after administration.
- Plasma volume increased substantially (> 40% in 3 cats)
- Analogous to the plasma volume expansion that accompanies uncontrolled diabetes mellitus in humans.

**MYTH** – That Cats are resistant to corticosteroid side effects

They just need higher doses to suppress allergy!

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Do Not Use !!!

- Dexamethasone to begin an anti-inflammatory course of prednisolone. No significant difference in onset of action.
- Depot corticosteroid injections of any sort in dogs.
  - Immunosuppressive
  - Cant be withdrawn
Corticosteroid Sprays

- Hydrocortisone aceponate 0.584 mg/ml (Cortavance®)
- Triamcinolone acetonide 0.015% (US-Genesis®) or compounded
- Compounded 0.025% budesonide in moisturizer
- Good efficiency
- Issues with dry or broken skin
- NOT a cure-all!
- NOT a free ride

Creams, ointments and Lotions

- Particularly with potent corticosteroids, risk of skin thinning and systemic absorption.
- Lower potency hydrocortisone preparations during maintenance

Colbetasol propionate 0.05% -0.1%
Mometasone 0.1% (Elcon), Betamethasone dipropionate (Diprosone)
Betametasone valerate (Celestone, Betnovate)
Triamcinolone (Panolog Aristocort)
Hydrocortisone
Cyclosporine

- Lag period of about 2-3 weeks
- 75-85% of cases get 75-85% better within 6 weeks

- Hepato/nephrotoxic side effects generally not recognized in dogs.
- Reversible gingival or cutaneous papilloma (more commonly bacterial, occasionally viral)
- Hirsutism
- Non interference with intradermal allergen testing
- Significant minority may go into remission if suspended.
- Used clinically in diabetic dogs

Cyclosporine inhibits cytokine production, especially interleukin-2
• Cyclosporine and Canine Atopic Dermatitis

• Perceived failures?
  • Trialed for < 6 weeks
  • Infection
  • Owner expectations and compliance
  • Tapering failures. 2 days on and 1 day off for 4 weeks BEFORE trying EOD
  • Something other that atopic dermatitis
  • One of the 25% that don’t respond

Vomiting and Cyclosporine

1. Give initially with food
2. If vomits, freeze capsule
3. If still vomits, ½ dose for 3 days and give metaclopramide 30 mins before.
4. Discontinue metoclopramide after 14 days

• Metoclopramide moderately increases cyclosporine blood levels and the food does not decrease clinical efficacy
Interactions with other drugs

**Cytochrome P450 3a**
- Catalyses metabolism of many drugs

**P-Glycoprotein**
- Active transport pump
- Gut, brain, kidney, liver

**Ketoconazole**
- 50-70% dose decrease @ 10mg/kg KTZ

**Ivermectin group**
- Death risk

**Phenobarbitone**
- induces hepatic Cyt P450 3a
- Decreases levels of Cs-A
- Increase dose Cs-A by 25%

Cyclosporine in Cats for Atopic Dermatitis

- FIV/FeLV negative
- No evidence of systemic disease
- Rule out of other pruritic diseases:
  - Flea allergy
  - Mites
  - Pyoderma & Malassezia
  - Food reactions
  - Dermatophytes
  - Pemphigus
  - Psychogenic
  - Neoplasia

- Very good response rate
- 25mg/cat daily for 1-2 months => every 2-3 days
- Monitor for infectious disease
- Widely used off label
- Much lower rate of serious side effects than corticosteroids (Diabetes, Heart Failure)
- Main reported side effects = GI disturbances and wt loss. Most cases not severe enough to stop usage
Cyclosporine and Feline Toxoplasmosis

- Uncommon complication
- New infections more important than re-activation of latent.
- Sero-negative cats at higher risk
- No evidence of re-shedding of oocysts. Only shed for a few weeks
- Cats that hyper-absorb cyclosporine at higher risk

- Prevent new infections
  - Cook meat
  - Stop hunting
  - Eliminate rodents

- 30 day CsA blood level
  - EDTA sample whole blood
  - 24 hours post pill
  - Should be 200-500ng/ml and not in 1000's

When do I use?

Prednisolone
- **Short term** to break itch scratch cycle
- **Pulse 3-5 days** for flares
- < 2x week in combo if NOTHING else works
- **Never alone**

Cyclosporine
- When **prednisolone reliant**
- **Severe cases awaiting allergen test**
- **Never alone.** Always part of combo

“The success of the treatment of 117 dogs with atopic dermatitis with allergen-specific immunotherapy for up to 48 months was assessed. An excellent response (remission with exclusive immunotherapy) was recorded in 18 of the dogs, a good response (more than 50 per cent reduction in medication and improvement of clinical signs) was recorded in 57, a moderate response was recorded in 24 and a poor response in 18.”

Atopic dermatitis and atopic-like dermatitis

• Not all dogs “atopic” dogs have demonstrated IgE against common environmental allergens

Prelaud 2007

• Food allergy excluded
• Typical signs
• Two negative intradermal tests
• Negative serological test
Allergen Specific Immunotherapy
ASIT

Set the goal posts: 2/3 get 50%+ better!

- The majority of cases will BENEFIT from ASIT BUT MAY require adjunct symptomatic therapy, including corticosteroids, for at least part of the year.
- Low cost means of long term control with minimal risks of side effects.
- Some cases may go into spontaneous remission

Infection Control- Vital!

- Infection significantly adds to the pruritus induced by allergy.
- In some cases, good infection control may be sufficient to keep the patient below the pruritic threshold.
- Atopic patients suffer from reoccurring infections because:
  - Increased bacterial adhesion
  - Altered local defense compounds and structure
  - Defective cell mediated immunity
  - Side effects of corticosteroids and cyclosporine(??)
  - Self trauma
Infections

Always scrape and tape

Every case
Be systematic
Tips for infection control

1. Treat any superficial bacterial/Malassezia infections systemically for at least 3 weeks or 10 days beyond clinical cure.
2. If bacterial infections re-occur straight away after systemic therapy, the duration of therapy may not have been long enough.
3. Reoccurrence 2-4 times a year best managed by repeated full course of antibiotics and topical therapy. More frequently re-occurring cases can be managed by weekend therapy.

Options for Malassezia treatment and control

- Topical miconazole (Daktarin ®), Hydrozole ® clotrimazole and hydrocortisone. Daily to treat, 2-3x week to hold
- Itraconazole (Sporonox ® ) 5-7mg/kg 2 consecutive days/week for 4 weeks
- Ketoconazole or Fluconazole 5-7mg/kg daily for 4 weeks
- 2% acetic acid wipes or footbaths

Malassezia hypersensitivity
- Demonstrated by ID test
- Immunotherapy
Systemic antibiotics for Pyoderma

First generation cephalosporins (e.g. cephalexin)
- Spectrum: gram positive bacteria, many anaerobes, some gram –v’s
- In Australia, low resistance S. pseudintermedius. Expect resistance to rise!
- The dermatology dose rate of cephalexin is 25mg/kg+ BID. Limited evidence 30mg/kg SID
- Moderately good intracellular penetration.
- About 5% of dogs will vomit on cephalexin.

Third generation cephalosporins Cefovecin (Convenia®)
- Wider activity against gram negative bacteria
- Blood levels above the MIC90 for cephalosporin susceptible stains of S. pseudintermedius for 14 days (in dogs and cats only) at the label dose.

Fluoroquinolones
- Resistance is rising.
- Ineffective against anaerobes and streptococci.
- Good penetration into skin
- Concentrated intracellularly.
- Activity related to peak blood levels, don’t divide the dose.
- Joint damage in growing dogs.
- Reserved for resistant cases where indicated by culture and sensitivity.

Amoxicillin clavulanate
- More costly.
- For ceph vomiting

Potentiated sulphonamides
- Previous high resistance
- Drug reactions (esp. Doberman).
- Renewed role in treating resistant staphylococci?

Lincomamides (lincomycin, clindamycin) Macrolides (clarithromycin azithromycin)
- 75% staphylococci sensitive.
- Good intracellular levels
- Bacteriostatic and resistance can develop quickly

Tetracyclines
- Bacteriostatic
- Poor penetration into skin.
- Moderate resistance
- Mildly immunosuppressant.
Hydration and restoring the epidermal barrier

Major cornerstone of managing human atopic dermatitis

Bricks and Mortar model of the Epidermis

- Surface hydrolipid film
- Keratinocytes in a “sea” of lipids
- Tight junctions between keratinocytes
- Adhesion and proliferation of microorganisms
- Ingress of allergens
- Drying via increased transepidermal water loss
Epidermal barrier defects: Primary or secondary?

**Genetics**
- Fifty-four genes differentially expressed in canine AD.

**Atopic dog skin has:**
- Decreased ceramide levels
- Increased cholesterol
- Disturbed extrusion of lamellar bodies by keratinocytes
- Increased trans-epidermal water loss
- Altered defensins

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**Stratum Corneum Lipids**

- 20% of volume of SC is lipid
- Sphingolipids 50%
- Cholesterol 25%
- Free fatty acids 10-20%

**Phytosphingosine**
- Mainly found in plants
- Occur in mammalian cells
- Similar properties (?)

**Sphingosine properties**
- Antimicrobial
- Barrier
- Immunomodulatory
Lipid Lamellae
Stratum Corneum
Marsalla 2010

Normal dog non-lesional stratum corneum.
Atopic dog non-lesional stratum corneum.

Abnormal structure exacerbated by allergen challenge

Moisturizers

Hygroscopic (humectant) agents
- Attract water into stratum corneum.
- Urea, glycerin, lactic acid and propylene glycol.

Emollients (Paraffin/mineral oil)
- Decrease epidermal water loss
- Form a barrier between skin and potential allergens.

Moisturizers
- Paws Nutriderm 1:2 spray
- Propylene glycol 25-33% spray
- Sorbolene (glycerin and paraffin oil + additives)
- Alpha Keri bath oil 1:50 spray

Bathing and wetting the skin
Benefit or harm (?)
Emollients may be MORE effective without bathing.
**Sphingolipid moisturizers**

Some studies in humans to indicate superiority

Optimal lipid balance yet to be determined in humans & dog.

Veterinary placebo controlled studies lacking

Good clinical results

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**0.025% BUDESONIDE Spray**

- Active steroid in Rhinocort spray
- Reduced systemic absorption?
- In 30% propylene glycol and 10% glycerin base
- Compounded
- Initial results = 1x week can maintain

Add 200ml tube to 400ml water.
Barrier Repair Therapy - Conclusions

- Topical and oral lipid complexes alter diseased skin structure and composition resulting in improved barrier function
  - Decreased doses of corticosteroids and cyclosporine
  - Increased immunotherapy efficiency
  - Decreased number of infections
  - Cost effective
  - Low toxicity
  - Not a monotherapy “cure”

Ancillary Therapy - Antihistamines

- Some dogs may respond to different antihistamines. Several may need to be trialed (individually) for 10-14 days.
- In the author’s experience, <10% of dogs show some response to antihistamines.
- Trial anti-histamines as a drug sparing agent once a base-line of control has been achieved with drug therapy and while awaiting the benefits of immunotherapy.
Ancillary Therapy – Essential fatty acids

- Optimal 3:6 ratio unknown
- Omega 6 improve barrier, Omega 3 anti-inflammatory
- Lower doses of drugs = decreased risk of side effects

- Don’t expect control with fatty acid therapy alone.
- A lag period of 6-12 weeks
- Synergism between fatty acid and antihistamines?

The “Neo-classical” Roadmap
Repeated courses of steroids
Now NOT on pred.
Signs fit Favot criteria

Elimination trial for fleas and sarcoptes
Treat secondary infections.
No topical or systemic steroids
Moisturize
Begin food trial

Allergen test within 2 - 3 weeks.

6-8 week food trial with RE-CHALLENGE
Steroids can be used intermittently but stop 10-14 days before re-challenge

Diagnosis of atopic dermatitis.
Make vaccine as part of treatment.
Thank you and any questions

✓ References available on request